UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,118	07/31/2003	Matthew B. Wheeler	99-02	1839

23713 7590 02/13/2007

GREENLEE WINNER AND SULLIVAN P C
4875 PEARL EAST CIRCLE
SUITE 200
BOULDER, CO 80301

EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,118	WHEELER ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed November 13, 2006 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-21 are pending.

This application has been transferred to Deborah Crouch, Ph.D.

New rejections are introduced in this office action rendering applicant's arguments moot. The arguments filed November 13, 2006 are not addressed.

The rejection under 35 U.S.C. § 112, first paragraph made in the office action mailed May 10, 2006 has been withdrawn in view of applicant's amendments to the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing because there is no method after "and" in step e. Also, the language of step b and step c are contradictory as to the temporal relationship between enucleation and activation.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 8, 14, 15 and 18 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sims et al. (1994) Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 6143-6147.

Sims teaches the production of calves by nuclear transfer where cultured ICM cells or ES cells were used as nuclear donor (page 6144, col. 2, parag. 2, lines 15-17 and figure 1;

and page 6145, col. 2, parag. 2, lines 1-7). First, NT embryos were produced, activated, cultured and transferred to surrogate female cows for term development of the calves (page 6146, col. 1, parag. 1 and 2). Sims further teaches enucleation of bovine oocytes by mechanical removal by a micropipette (page 6144, col. 1, parag. 2, lines 11-27). Reconstituted embryos were fused by either polyethylene glycol (PEG) or electrofusion (page 6144, col. 2, parag. 1, lines 1-6). Thus, Sims clearly anticipates the claimed invention.

Claims 1 and 13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Wakayama et al (1998) Proced. Natl. Acad. Sci. USA, Vol. 96, pp. 14984-14989.

Wakayama teaches the production of mice by nuclear transfer of an ES cells nucleus into an enucleated MII oocyte, where the nucleus is transferred by piezo-directed microinjection (page 14985, col. 1, parag. 2). The reconstituted embryos are developed to the blastocyst stage and transferred to the uterus of a female mouse for term development (page 14986, col. 2, parag. 2, lines 2-6). Thus, Wakayama clearly anticipates the claimed invention.

Claims 1, 4, 15 and 17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Amano et al. (2001) Reproduction, Vol. 121, pp. 729-733.

Amano teaches the production of mice by nuclear transfer using mouse ES cells as nuclear donor, where the nucleus is fused to an enucleated oocyte by Sendai virus (page 729, col. 2, parag. 2, lines 5-11). In particular, Amano teaches transgenic mouse ES cells as nuclear donors. Thus Amano clearly anticipates the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

> matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheeler (1994) Reprod. Fertil. Dev., Vol. 6, pp. 563-568 in view of Sims et al. (1994) Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 6143-6147.

Wheeler teaches the use of pig ES cells as nuclear donors in cloning methods whereby a pig ES cells is fused or injected with or into enucleated oocytes (col. 22, lines 11-15). Wheeler teaches the production of pig ES cells (col. 10, line 34 to col. 14, line 58) and their use in the production of chimeric pigs using Meshian embryos as recipient (page 565, parag. 1). Wheeler further teaches the production of transgenic pigs expressing Factor IX in their milk by electroporating an FIX DNA sequence ligated to an α-lactalbumin promoter into pig ES cells (col. 19, lines 46-59). Wheeler offers motivation in stating pig ES cells offer a means to produce transgenic pigs for the production of pharmaceuticals or organs for transplantation therapies (col. 5, lines 16-25).

Sims teaches the production of calves by nuclear transfer where cultured ICM cells or ES cells were used as nuclear donor (page 6144, col. 2, parag. 2, lines 15-17 and figure 1; and page 6145, col. 2, parag. 2, lines 1-7). Sims offers motivation in stating the use of ES cells in gene transfer could be more efficient as cells could be selected for gene integration or expression prior to the production of transgenic offspring (page 6146, col. 2, parag. 6, lines 5-7).

Therefore at the time of the instant invention, it would have been obvious to the ordinary artisan to produce a pig by nuclear transfer using a transfected pig ES cells as nuclear donor into an enucleated pig oocyte as taught by Wheeler in view of Sims teaching the production of cloned bovines using bovine ES cells as nuclear donors, and Sims additionally teaching the ES cells can be transfected.

Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wakayama et al (1998) Proced. Natl. Acad. Sci. USA, Vol. 96, pp. 14984-14989 in view of Fulka Jr et al (1993) Mol. Reprod. Devel., Vol. 34, pp. 427-430 (Fulka).

Wakayama teaches the production of mice by nuclear transfer of an ES cells nucleus into an enucleated MII oocyte, where the nucleus is transferred by piezo-directed microinjection (page 14985, col. 1, parag. 2). The reconstituted embryos are developed to the blastocyst stage and transferred to the uterus of a female mouse for term development (page 14986, col. 2, parag. 2, lines 2-6). Wakayama teaches physical enucleation of mouse oocytes (page 373, col. 2, lines 5-12).

Fulka teaches the nucleation of mouse oocytes undergoing germinal vesicle breakdown by incubation in etoposide followed by incubated in etoposide and cycloheximide (page 427, col. 2, parag. 1, lines 7-16). Fulka offers motivation for the etoposide-cycloheximide enucleation technique in stating that it is a simple method having the capacity to enucleate large numbers of oocytes at the same time, while permitting exposure of the donor nucleus to MPF prior to activation for a long period of time (page 430, col. 1, lines 5-12).

Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to modify the nuclear transfer method of Wakayama, where mouse oocytes were enucleated by micropipette aspiration, with the method of Fulka to chemically enucleated mouse oocytes by a simplistic method. The cited prior art provides the requisite teachings, suggestion and motivation to combine.

Claims 1, 6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al. (1994) Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 6143-6147 in view of Bradshaw et al (1995) Mol. Reprod. Devel. 41, pp. 503-512.

Sims teaches the production of calves by nuclear transfer where cultured ICM cells or ES cells were used as nuclear donor (page 6144, col. 2, parag. 2, lines 15-17 and figure 1; and page 6145, col. 2, parag. 2, lines 1-7). First, NT embryos were produced, activated, cultured and transferred to surrogate female cows for term development of the calves (page 6146, col. 1, parag. 1 and 2).

Bradshaw teaches the enucleation of bovine gv and MII oocytes by exposure to UV-C irradiation at 254 nm (page 505, col. 1, parag. 2, lines 1-5). Bradshaw teaches the exposure prevents the formation of a metaphase plate or a polar body in gv oocytes (page 505, col. 1, parag. 8, lines 1-3) and prevents the formation of a pronucleus (page 505, col. 2, parag. 5, lines 3-8). Bradshaw further teaches UV-C irradiation is a potential means for oocyte enucleation (page 503, abstract, lines 18-19).

Thus, at the time of filing, it would have been obvious to the ordinary artisan to modify the method taught by Sims, where oocytes were enucleated by physical means, with enucleation by uV irradiation at 254 nm, as taught by Bradshaw, to improve rates of blastocyst development. The cited prior art provides the requisite teachings, suggestions and motivation to combine.

Claims 1, 6, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims et al. (1994) Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 6143-6147 in view of Tatham et al (1995) Bio. Reprod. 53, 1088-1094.

Sims teaches the production of calves by nuclear transfer where cultured ICM cells or ES cells were used as nuclear donor (page 6144, col. 2, parag. 2, lines 15-17 and figure 1; and page 6145, col. 2, parag. 2, lines 1-7). First, NT embryos were produced, activated,

cultured and transferred to surrogate female cows for term development of the calves (page 6146, col. 1, parag. 1 and 2).

Tatham teaches the enucleation of bovine oocytes by density gradient centrifugation using Percoll as the centrifugation media (page 1089, col. 1, parag. 3, lines 3-7). Motivation is provided by Tatham stating enucleation by centrifugation is fast and easy, and provides the same number of morula as micromanipulation enucleation (page 1093, col. 2, parag. 1, lines 4-9 and parag. 2, lines 5-8).

Thus at the time of filing, it would have been obvious to the ordinary artisan to modify the enucleation method of Sims with the enucleation by centrifugation method of Tatham to simply nuclear transfer. The cited prior art provides the requisite teachings, suggestions and motivation to combine.

Claims 1, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amano et al. (2001) Reproduction, Vol. 121, pp. 729-733.

Amano teaches the production of mice by nuclear transfer using mouse ES cells as nuclear donor, where the nucleus is fused to an enucleated oocyte by Sendai virus (page 729, col. 2, parag. 2, lines 5-11). In particular, Amano teaches transgenic mouse ES cells as nuclear donors. However, Amano does not teach Sendai virus. At the time of filing, alphavirus was known to have fusogenic properties. As the level of experimentation was high in nuclear transfer, it would have been obvious to the ordinary artisan at the time of filing to fuse a donor mouse ES cells with a mouse oocyte using an alphavirus to replace a Sendai virus. The cited prior art provides the requisite teachings, suggestions and motivation to combine.

Claims 1, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheeler (1994) Reprod. Fertil. Dev., Vol. 6, pp. 563-568 and Prather et al (1989) Bio. Reprod., Vol. 41, pp. 414-418 in view of Sims et al. (1994) Proc. Natl. Acad. Sci. USA, Vol. 91, pp. 6143-6147.

Wheeler teaches the use of pig ES cells as nuclear donors in cloning methods whereby a pig ES cells is fused or injected with or into enucleated oocytes (col. 22, lines 11-15). Wheeler teaches the production of pig ES cells (col. 10, line 34 to col. 14, line 58) and their use in the production of chimeric pigs using Meshian embryos as recipient (page 565, parag. 1).

Prather teaches the production of a cloned piglet by nuclear transfer where a Yorkshire X Landrace pig oocyte was the recipient cell of a Yorkshire X Landrace pig blastomere (page 424, col. 2, parag. 2, line 1 to page 425, col. 1, line 2). The oocytes were enucleated by removal of the first polar body and cytoplasm underneath and the donor nucleus transferred, followed by electrofusion (page 415, col. 1, parag. 2, to col. 2, parag. 2). Prather teaches the production 2-,4-, 8- cell stage embryos and compact morula and expanded blastocyst formation (page 416, col. 1, parag. 2). However, Prather does not teach the production of pigs by nuclear transfer using ES cells as nuclear donor.

Sims teaches the production of calves by nuclear transfer where cultured ICM cells or ES cells were used as nuclear donor (page 6144, col. 2, parag. 2, lines 15-17 and figure 1; and page 6145, col. 2, parag. 2, lines 1-7). First, NT embryos were produced, activated, cultured and transferred to surrogate female cows for term development of the calves (page 6146, col. 1, parag. 1 and 2). Sims further teaches enucleation of bovine oocytes by mechanical removal by a micropipette (page 6144, col. 1, parag. 2, lines 11-27). Reconstituted embryos were fused by either polyethylene glycol (PEG) or electrofusion (page 6144, col. 2, parag. 1, lines 1-6).

Wheeler offers motivation in stating pig ES cells offer a means to produce transgenic pigs for the production of human proteins for the treatment of genetic or other diseases, and as source of organs for transplantation therapies (page 564, col. 1, parag. 1, lines

21033). Sims offers motivation in demonstrating the production of cloned calves (page 6143, col. 2, parag. 3).

Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to produce cloned pigs by nuclear transfer, comprising modifying the method of Prather by using transgenic pig ES cells as taught by Wheeler as nuclear donor as taught by Sims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

January 29, 2007